

WHAT IS CLAIMED IS;

1 1. A process for producing one or more human monoclonal
2 antibodies which bind specifically to Shiga toxin or Shiga-like
3 toxin, which comprises the following steps:

4 (1) administering Shiga-like toxoid I or Shiga-
5 like toxoid II as an antigen to a transgenic mouse having human
6 genes and inducing an immune response in the transgenic mouse;

7 (2) isolating splenocytes from the transgenic
8 mouse following an immune response by the transgenic mouse and
9 fusing the splenocytes to mouse myeloma cells to obtain mouse
10 hybridomas producing human monoclonal antibodies; and

11 (3) screening the human monoclonal antibodies
12 to obtain the human monoclonal antibodies which bind specifically
13 to Shiga toxin or Shiga-like toxin.

1 2. The process for producing one or more human
2 monoclonal antibodies defined in claim 1 wherein the human
3 monoclonal antibodies which bind specifically to Shiga toxin or
4 Shiga-like toxin bind to Shiga-like toxin I.

1 3. The process for producing one or more human
2 monoclonal antibodies defined in claim 1 wherein the human
3 monoclonal antibodies which bind specifically to Shiga toxin or
4 Shiga-like toxin bind to Shiga-like toxin II.

1 4. The process for producing one or more human
2 monoclonal antibodies defined in claim 1 wherein the human
3 monoclonal antibodies which bind specifically to Shiga toxin or
4 Shiga-like toxin bind to Shiga toxin.

1 5. The process for producing one or more human
2 monoclonal antibodies defined in claim 1 wherein according to step
3 (1) the transgenic mouse having human genes is capable of
4 expressing a diversity of human heavy and light chain
5 immunoglobulins.

1 6. The process for producing one or more human
2 monoclonal antibodies defined in claim 1 wherein according to step
3 (1) the transgenic mouse having human genes is capable of
4 expressing unrearranged human heavy and light chain
5 immunoglobulins.

1 7. The process for producing one or more human
2 monoclonal antibodies defined in claim 1 wherein according to step
3 (1) the Shiga-like toxoid I or Shiga-like toxoid II antigen is
4 intraperitoneally administered in an amount of 20 to 100 μ g on day
5 1 to the transgenic mouse in complete Freund's adjuvant followed by
6 weekly intraperitoneal immunizations with 5 to 20 μ g of antigen in
7 incomplete Freund's adjuvant.

1 8. A human monoclonal antibody which binds specifically
2 to Shiga toxin or Shiga-like toxin prepared by the process defined
3 in claim 1.

1 9. The human monoclonal antibody defined in claim 8 that
2 specifically binds to Shiga-like toxin II as the Shiga-like toxin.

1 10. The human monoclonal antibody defined in claim 9
2 that specifically binds to the A-subunit of Shiga like toxin II.

1 11. The human monoclonal antibody defined in claim 9
2 that specifically binds to the A-subunit of Shiga like toxin II and
3 that neutralizes multiple variants of Shiga likme toxin II.

1 12. The human monoclonal antibody defined in claim 8
2 that specifically binds to various clinical variants of Shiga-like
3 toxin II as the Shiga-like toxin.

1 13. The human monoclonal antibody defined in claim 9
2 that specifically binds to Shiga-like toxin II and which is
3 selected from the group consisting of 5C12 and 3E9.

1 14. The human monoclonal antibody defined in claim 8
2 that specifically binds to Shiga-like toxin I as the Shiga-like
3 toxin.

15. The human monoclonal antibody defined in claim 8 that specifically binds to various clinical variants of Shiga-like toxin I as the Shiga-like toxin.

16. The human monoclonal antibody defined in claim 8 that will not elicit reaction in humans to foreign proteins.

17. A therapeutic method of treating an individual for hemolytic uremic syndrome or of protecting an individual against hemolytic uremic syndrome, said method comprising the steps of:

(a) producing one or more human monoclonal antibodies which bind specifically to Shiga toxin or Shiga-like toxin, said human monoclonal antibodies which bind specifically to Shiga toxin or Shiga-like toxin obtained by the following steps:

(1) administering Shiga-like toxoid I or Shiga-like toxoid II as an antigen to a transgenic mouse having human genes and inducing an immune response in the transgenic mouse;

(2) isolating splenocytes from the transgenic mouse following an immune response by the transgenic mouse and fusing the splenocytes to mouse myeloma cells to obtain mouse hybridomas producing human monoclonal antibodies; and

(3) screening the human monoclonal antibodies to obtain the human monoclonal antibodies which bind specifically to Shiga toxin or Shiga-like toxin; and

18 (b) administering the human monoclonal antibodies which
19 bind specifically to Shiga toxin or Shiga-like toxin to the
20 individual in a therapeutically effective amount.

1 18. The therapeutic method defined in claim 17 wherein
2 the human monoclonal antibodies which bind specifically to Shiga
3 toxin or Shiga-like toxin bind to Shiga-like toxin I.

1 19. The therapeutic method defined in claim 18 wherein
2 the human monoclonal antibodies which bind specifically to Shiga
3 toxin or Shiga-like toxin bind to Shiga-like toxin II.

1 20. The therapeutic method defined in claim 18 wherein
2 the human monoclonal antibodies which bind specifically to Shiga
3 toxin or Shiga-like toxin bind to Shiga toxin.

1 21. The therapeutic method defined in claim 17 wherein
2 the hemolytic uremic syndrome is caused by a Shiga-like toxin
3 producing bacteria.

1 22. The therapeutic method defined in claim 21 wherein
2 the Shiga-like toxin producing bacteria is Enterohemorrhagic
3 Escherichia coli.

1 23. The therapeutic method defined in claim 17 wherein
2 the individual is protected from hemolytic uremic syndrome through
3 passive immunization by administering to the individual a
4 prophylactically effective amount of the human monoclonal
5 antibodies which bind specifically to Shiga toxin or Shiga like
6 toxin.

1 24. The therapeutic method defined in claim 19 wherein
2 the human monoclonal antibodies which bind specifically to Shiga
3 like toxin II specifically bind to the A-subunit of Shiga like
4 toxin II.

1 25. The therapeutic method defined in claim 19 wherein
2 the human monoclonal antibodies which bind specifically to Shiga
3 like toxin II specifically bind to the A-subunit of Shiga like
4 toxin II and neutralize multiple variants of Shiga like toxin II.